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Abstract

Background and aims: In Scotland, HBV vaccination for all prisoners was introduced in 1999; here, we examine the impact of this programme among people who inject drugs (PWID) in the community. This study aimed to compare rates of HBV vaccine uptake before and after implementation of the prison programme and to estimate the determinants of vaccine uptake, the levels of ever/current HBV infection and the associations between vaccine uptake and ever/current HBV infection.

Design: Data collected via serial cross-sectional surveys were used to compare the proportion who reported being vaccinated over time. For the 2013-14 survey, rates of ever/current HBV infection were calculated and the associations between vaccine uptake and ever/current HBV infection were examined using logistic regression.

Setting: Services providing injecting equipment and drug treatment, and street sites, in Glasgow (1993–2002) and across Scotland (2008–2014).

Participants: More than 10,000 PWID in total were recruited in the surveys.

Measurements: Participants completed a questionnaire (all years) to ascertain self-reported vaccine uptake and provided a blood spot (in 2013-14), tested for HBV core antibodies (anti-HBc) and surface antigen (HBsAg).

Findings: Among recent-onset PWID in Glasgow, vaccine uptake increased from 16-20% in 1993-99 to 52-59% in 2001-2014 ($p<0.001$). Among all PWID in Scotland, uptake increased further from 71% in 2008-09 to 77% in 2013-14 ($p<0.001$) and was associated with incarceration (adjusted odds ratio 2·91, 95% CI 2·23-3·79). The prevalence of anti-HBc and HBsAg in Scotland was 2·6% and 0·3%, respectively, among PWID who had commenced injecting in the decade since the programme's introduction. Vaccination was associated with reduced odds of ever (0·60, 0·37-0·97) and current (0·40, 0·16-0·97) HBV infection.

Conclusions: In Scotland, uptake of HBV vaccination among PWID in the community has continued to increase since the introduction of universal prison vaccination, and levels of HBV infection among PWID are low.

Abstract word count: 300

Key words: hepatitis B, injecting drug use, prison, vaccination, immunisation

INTRODUCTION

The Hepatitis B virus (HBV) is a blood-borne virus that can cause serious morbidity, including cirrhosis and hepatocellular carcinoma. In areas of low HBV prevalence, injecting drug use is one of the main risk factors for acquiring the virus [1]. There are an estimated 12 million people who inject drugs (PWID) worldwide [2], 6·4 million and 1·2 million of whom are estimated to be positive for HBV antibodies (anti-HBc) and HBV surface antigen (HBsAg), respectively [1].

The World Health Organization (WHO) global hepatitis strategy [3]was endorsed at the World Health Assembly in May 2016, where countries committed to eliminating HBV as a public health threat, with targets to reduce HBV incidence by 95% by 2030 [4]. An effective vaccine to prevent HBV infection is available and universal vaccination of infants had been implemented in 184 countries worldwide as of 2014 [5,6]. Consequently, rates of chronic infection are extremely low among vaccinated cohorts [7]. Nevertheless, HBV transmission among PWID remains a concern given that, for most countries, the birth cohorts that have been vaccinated have not reached the average age of injecting onset. The impact of catch-up programmes and additional efforts to target at-risk population groups may be limited by inequitable uptake and/or incomplete coverage. Thus, HBV transmission among PWID is ongoing in many countries [8-11]: for example, in the United States, where universal vaccination of infants began in 1991 [12], there are currently an estimated 19,000 cases of acute HBV infection annually, with 26% of reported cases (with a known risk factor) attributable to injecting drug use [13]. In countries of the European Union/European Economic Area, injecting drug use accounts for 15% of reported acute HBV cases [14].

A minority of countries, including the United Kingdom (UK), have instead taken a targeted approach, whereby only selected groups at high risk of exposure to HBV are offered vaccination – including PWID [6,15]. High HBV vaccine uptake among PWID can be difficult to achieve through community-based programmes [11]. Given that many PWID are incarcerated early in their injecting careers, and they frequently transition into and out of prison [16], prisons can be ideal settings for public health interventions targeting this hard-to-reach group.

HBV vaccination for all prisoners was introduced in Scottish prisons in 1999, following regional and prison-related outbreaks of acute HBV among PWID [17]. More than 15 years have now elapsed since the introduction of the prison programme and, given the UK is one of the few countries that have not implemented universal infant vaccination, there is a unique opportunity to evaluate its effectiveness.

In this study, we consider the evidence that the Scottish prison vaccination programme was associated with changes in uptake of HBV vaccination and markers of HBV infection among PWID recruited at community sites across Scotland. Specifically, the aims of this study were to (1) compare rates of HBV vaccine uptake before and after implementation of the prison programme, (2) to identify the determinants of vaccine uptake (including incarceration), (3) to estimate the prevalence of ever and current HBV infection and (4) to estimate the association between vaccine uptake and ever/current HBV infection, among PWID in the community. To our knowledge, this is the first national study of a universal prison vaccination programme in terms of both vaccine uptake and infection among PWID [17,18].

METHODS

Design

The study consists of a series of cross-sectional surveys of PWID, initially confined to Glasgow then later expanded to cover all of mainland Scotland. The changes in vaccine uptake for Glasgow were compared across the surveys. Scotland data were subsequently pooled to examine determinants of vaccine uptake. Levels of HBV infection and the association between vaccine uptake and infection were examined at Scotland-level for 2013-14.

Study sample

The surveys were undertaken in Glasgow in 1993, 1994, 1999 and 2001-02, and across mainland Scotland (including Glasgow) in 2008-09, 2010, 2011-12 and 2013-14. All surveys were undertaken by trained interviewers. Informed consent was obtained from participants

and the studies were approved by the West of Scotland Research Ethics Service. The survey methods have also been described elsewhere [19-22].

Glasgow surveys (1993 to 2002)

The sampling frame consisted of 15 injecting equipment provision (IEP) services, 20 drug treatment services and numerous street sites located throughout Glasgow. Recruitment at IEP and drug treatment services was rotated by day of the week and time of day to capture as representative a sample as possible: all potentially eligible individuals attending these sites were approached to participate. Street sites were chosen in areas of high deprivation, which were more likely to have a higher prevalence of injecting drug use. Interviewers approached each person that passed by, gave a brief description of the study and asked "we are looking for injecting drug users, do you know of anyone who may like to take part in the study?" The 1993 and 1994 surveys were restricted to people who had injected drugs in the two months prior; in 1999, respondents were eligible if they had injected since January 1990.

Scotland surveys (2008 to 2014)

The sampling frame in each national survey consisted of approximately 100 IEP sites (some of these may also provide drug treatment), which constitutes approximately 40-50% of all IEP sites across Scotland. Sites were chosen to be broadly geographically representative of the regional administrative health areas (NHS Boards), comprising a mixture of urban and rural sites. Interviewers rotated days of the week and times of day at which they recruited from the sites; all individuals attending the service were approached to participate. Target sample sizes were set for each NHS Board based on existing knowledge of the size of the injecting population in each. Recruitment in each NHS Board took place over a period of approximately six weeks, although more or less time may have been required in order to achieve the target. People who had ever injected were eligible for participation (although the proportion of respondents who had injected in the last six months was maintained at a minimum of 75%). Participants were also asked to provide a blood spot sample for blood-borne virus testing.

Laboratory testing

HBV testing was performed on dried blood spots (DBS) from the 2013-14 survey. Samples were tested for anti-HBc; those that tested positive were then tested for HBsAg. DBS were eluted using a modified version of a published method [23]. The modifications were two 3mm discs punched from the DBS and eluted in 200µl of PBS/tween 0.05%. The eluates were tested on the Abbott Architect i2000sr using the following assays: Architect Hepatitis B core II antibody, Architect HBsAg Qualitative II assay and Architect HBsAg Confirmatory assay. Low-level HBsAg positive samples that could not be verified by neutralisation on the Architect were confirmed using the miniVIDAS HBsAg Ultra assay (bioMérieux). The sensitivity of the DBS method (compared to plasma) for anti-HBc and HBsAg detection is 89·8% (95% CI 77·8-96·6%) and 100% (95% CI 90·5 – 100%), respectively. The specificity for anti-HBc and HBsAg DBS testing is 100% (95% CI 81·5-100%) and 81·8% (95% CI 59·7-94·8%), respectively. The sensitivity and specificity of HBsAg confirmation testing was 100% (95% CI 90·0-100%). Individuals who were anti-HBc positive were considered to be 'ever infected'; past infection was defined as being anti-HBc positive and HBsAg negative; and current infection was defined as being anti-HBc and HBsAg positive.

Statistical analysis

Trends in vaccine uptake

The proportions of respondents reporting having been vaccinated (received at least one dose), having received 3+ doses of the vaccine, and having been vaccinated in various settings were compared across the surveys. This was done separately for Glasgow and Scotland. Chi-square tests and p-values were calculated.

(i) Glasgow

The proportions above were compared for Glasgow across the time period 1993 through 2014. The data from the Scotland surveys (2008-09 to 2013-14) were restricted to those recruited in Greater Glasgow & Clyde who had been injecting for less than five years and who had injected in the last six months (while it was not possible to restrict to the last two months, we looked at restricting to the last month and this made no difference to the results). This was done to enable a valid comparison, given the different eligibility criteria

applied in the Glasgow surveys (see above). In this analysis, the 2008-09 to 2013-14 data were collapsed, as it was found not to have changed across these four surveys.

(ii) Scotland

These same proportions described above were also compared across the four national surveys for all PWID respondents.

Determinants of vaccine uptake

The difference in self-reported vaccine uptake across the national surveys (2008-09 to 2013-14), and according to whether ever incarcerated, was assessed using logistic regression adjusted for potentially confounding factors (gender, age at interview, time since onset of injecting, and ever prescribed methadone). These analyses were restricted to those with less than ten years since injecting onset, the rationale being that these individuals had commenced injecting following the introduction of the prison programme. It was not feasible to take account of variation across the hundreds of sites where recruitment took place; however, we considered potential clustering by recruitment region (i.e. NHS Board areas, which are administrative authorities of the Scottish health service who manage local services for PWID, including prevention of blood-borne viruses). To achieve the latter, a multi-level framework was applied to the logistic regression model to take into account potential variation by NHS Board.

Prevalence of ever and current HBV infection

For the 2013-14 survey, the prevalence of ever infection (anti-HBc positivity) and current infection (i.e. those positive for anti-HBc *and* HBsAg) were calculated for all respondents and for those with less than 10 years since onset of injecting.

Association between HBV vaccination and infection

Given that vaccination may not have an impact if it is delivered after infection has occurred, it is important to demonstrate this effect. Among participants whose DBS samples had been tested for HBV, the association between having been vaccinated for HBV (self-reported) and ever infection was explored. Potential confounding factors (gender, age, time since onset of

injecting and having been incarcerated) were identified *a priori*, and fitted into a logistic regression model with the dependent and independent variables. A multi-level model, to take into account clustering by NHS Board (as described above) was applied.

A similar approach to that described above was used to explore the association between HBV vaccination and current HBV infection. Currently infected individuals were compared to those negative for anti-HBc. The same confounding factors listed above were examined in multivariable models. While it was not possibly to apply a multi-level model due to too few observations per cluster, NHS Board was included in the model as a potential confounder (and collapsed into Greater Glasgow & Clyde NHS Board vs. elsewhere).Analyses were undertaken in SPSS version 21, EpiInfo 7 and R version 3.2.3.

RESULTS

Trends in vaccine uptake (Glasgow 1993-2014)

Among recent-onset PWID in Glasgow, there was a significant upward trend ($p<0{\cdot}001$) in vaccination uptake across the period beginning prior to introduction of the prison programme (16% in 1993) up until the more recent surveys (59% in 2008-14, see Table 1 and Figure 1). Among those vaccinated, the proportion who reported receiving 3+ doses of the vaccine increased from 62% to 81% ($p<0{\cdot}001$) between 2001-02 and 2008-14. Since the introduction of the prison programme, prisons were where the largest proportion of vaccinations took place (56% and 40% of vaccinations in 2001-02 and 2008-14, respectively).

[insert Figure 1 and Table 1 here]

Trends in vaccine uptake (Scotland 2008-14)

At the Scotland level, there was a significant increase ($p<0{\cdot}001$) in self-reported vaccine uptake across the four surveys, from 71% to 77% (Table 1). Among those who reported having been vaccinated, there was also a significant increase in the proportion reporting having received 3+ doses (from 77% to 83%, $p<0.001$). Although small changes occurred in general practice and drug treatment settings, the largest proportion of vaccinations took place in the prison setting (41% in 2013-14).

Determinants of vaccine uptake (Scotland 2008-14)

Among those who had been incarcerated since their injecting debut, 83% had been vaccinated for HBV, as compared with 58% of those who had not been incarcerated (Table 2). After adjustment, the following were significantly associated with vaccine uptake: aged >35 years at interview (with this group having lower uptake, as compared to those aged ≤25; time since onset of injecting (with those who had been injecting longer having higher odds of vaccine uptake); having been prescribed methadone and having been incarcerated (with both prescribed methadone and past incarceration being associated with approximately 3-fold increased likelihood of vaccine uptake).

[insert Table 2 here]

Prevalence of ever and current HBV infection (Scotland 2013-14)

At the Scotland level, the prevalence of anti-HBc was 9% (210/2322) and the prevalence of HBsAg was 0·9% (22/2322). Among PWID who had commenced injecting in the previous ten years, the prevalence of anti-HBc and HBsAg was 2·6% (23/872) and 0·3% (3/871), respectively.

Association between HBV vaccination and infection (Scotland 2013-14)

After adjustment for potentially confounding factors, having been vaccinated for HBV was associated with a lower odds of being anti-HBc positive, as compared to non-vaccinees (Table 3). We also examined separately the odds of anti-HBc positivity among those vaccinated outside of prison and those vaccinated in prison and found that the AORs for the latter and the former were 0.61 (95% CI 0.40-0.94) and 0.57 (0.31-1.06), respectively, relative to those never vaccinated.

[insert Table 3 here]

Those who had been vaccinated for HBV were also significantly less likely to have a current HBV infection, after adjustment for potential confounders (Table 4).

[insert Table 4 here]

DISCUSSION

We found that HBV vaccination uptake among recent-onset PWID has continued to increase since the period before, and shortly after, the introduction of universal prison vaccination, and that vaccination is associated with a reduced risk of HBV infection.

While the pre-prison programme data correspond to Glasgow, it is reasonable to assume that the trend will have been replicated across Scotland, given the parallels between the Glasgow and Scotland data (Figure 1). We also found that, at the national level, vaccine uptake among PWID has increased over the period 2008 to 2014, with more than 75% of respondents reporting having received at least one dose of the vaccine in 2013-14. Importantly, among recent-onset injectors in Glasgow (who are prime targets for vaccination because they are less likely to be infected at the beginning of their injecting careers), there was a rise in the proportion of those vaccinated receiving at least 3 doses of the vaccine (to 81% in 2013-14), up from 62% in 2001-2002.

Incarceration was associated with an increased uptake of vaccination: 83% of PWID who had been incarcerated reported receiving the vaccine (compared to 64% among incarcerated individuals in 2001-02) [17], suggesting the vaccination programme is capturing an appreciable number of PWID who are imprisoned. (Potential reasons for <100% coverage among those who report having been incarcerated are: all new admissions are offered immunisation but some decline; a number of those committed to prison would have been released before vaccination could have been arranged; and some prisoners may have received the vaccine on admission but may simply have inaccurate recall). Given the observational nature of this study, we cannot infer a causal association between the prison programme and our finding of increased vaccine uptake; however, prison is the most common site where PWID report receiving vaccinations (ranging from 40-50% in recent years) and, with no appreciable change in other settings, it is therefore unlikely that vaccination uptake rates of nearly 80% in the community would have been achieved without the prison programme. However, we do not know whether multiple doses from the vaccine schedule were received in prison, at other sites, or indeed across sites.

Our analysis indicated that vaccination was associated with a reduced risk of infection. While this may be expected, it is nevertheless important to demonstrate this effect, given that vaccination may not necessarily be effective if it is delivered at the wrong time – for example, an individual may have acquired infection prior to receiving vaccination (particularly given that the highest risk of infection is in the first few years of injecting and therefore may occur before any contact with the prison service). In this study, the prevalence of infection among those who report having been vaccinated was 8.3% for anti-HBc and 0.9% for HBsAg. Potential reasons for this finding (other than becoming infected prior to vaccination) include: incomplete immunity due to not receiving the entire vaccine series; or potentially incorrect recall. Nevertheless, this finding highlights a potential gap for the prison programme as a public health strategy.

We also found that incarceration was associated with an increased risk of infection, a finding that is consistent with other studies [11,24]. This observation is likely explained by the possibility that respondents may have become infected with HBV before imprisonment (and imprisonment may be a proxy for risk, i.e. individuals who end up in prison may also engage in more risk behaviours that expose them to HBV).

This study established that the prevalence of anti-HBc and HBsAg is currently low among PWID in Scotland, particularly among those who had commenced injecting after the introduction of the prison programme. The overall prevalence of anti-HBc among Scottish PWID (9%) is lower than that reported in other European countries (lower than 22 out of 25 countries in a recent review) [1]; similarly the prevalence of HBsAg (0·9%) is lower than that reported by 15 out of 20 countries in another review [25]. The low levels of these HBV markers are consistent with data on acute HBV infections in Scotland, which have been declining and are at an all-time low. The number of acute infections reported annually has declined from 162 cases in 1999 (38% of whom were known to have injected drugs) to less than 20 cases in 2015 (none of which had injecting drug use indicated as a risk factor, although half had no risk information) [26]. The indication is that levels of HBV transmission among PWID in Scotland are very low indeed.

Given the observational nature of this study, we cannot attribute the low levels of HBV infection solely to vaccination uptake: these are likely partly attributable to a range of other

interventions that have been scaled up in Scotland since the early 1990s, including sterile injecting equipment provision and opiate substitute therapy. However, further evidence to support the effectiveness of prison vaccination is that there have been no outbreaks of HBV among PWID since the introduction of the prison programme (personal communication, David Goldberg), whereas there had been several outbreaks just prior to its introduction [27,28].

Some key elements of the Scottish prison programme that likely contributed to its success were: not testing initially for evidence of previous exposure or immunity, adoption of the accelerated schedule (0, 1, and 2 months, and 6 month booster), and not testing for titre levels following vaccination. These elements helped to ensure the programme was easy to implement and achieved the greatest level of herd immunity possible in a transient population (personal communication, Alan Mitchell, former Head of Healthcare in the Scottish Prison Service). Additionally, all prisoners were encouraged to get immunised regardless of injecting history, which reduced stigma. A recent HBV transmission event in an English prison related to tattooing highlights the potential wider benefit of this approach [29].

In this paper, we have examined over 20 years of data on the uptake of HBV vaccination and recent data on markers of HBV infection among PWID recruited in Scotland in order to assess the potential impact of the Scottish HBV prison vaccination programme, established in 1999. Given the UK is one of the few countries that have not implemented universal infant or adolescent HBV vaccination [6], there is a unique opportunity to evaluate this programme because the effects of the programme have not been contaminated by universal infant vaccination or catch-up programmes. However, the findings of this study are pertinent not just to other countries that have not implemented universal infant vaccination, but also to countries that have. This is because these programmes may not have had sufficient time to reach maturity. Assuming the average age of injecting debut is approximately 20 years, countries would have had to implement universal infant vaccination in 1996 or earlier, so that the birth cohorts that are now approaching the age of injecting onset are protected against HBV; however, less than a third of member states are in this situation [6]. Hepatitis B vaccines first became available in the early 1980s [30], so even the earliest adopters would

only have coverage of cohorts up to age 35. Therefore, given the need for supplementary vaccination strategies to target PWID, and given that most countries have high rates of imprisonment of PWID [31], universal vaccination of prisoners presents an effective method of capturing this 'hard-to-reach' population.

Limitations of this study

The study sample for these analyses was drawn, in the main, from settings providing harm reduction services, which may under-represent PWID who are not in contact with such services. However, previous community-wide surveys undertaken in Glasgow showed that 90% of PWID recruited from street sites had visited IEP services in the past six months [22] and we would therefore expect the study sample to reflect the great majority of PWID.

Regarding the sensitivity of the laboratory tests, we may have missed anti-HBc and/or HBsAg infections (i.e. false negatives), which would result in an underestimate of the prevalence of these markers; however, these are likely to be few in number given that the prevalence of these markers is low. If the specificity of the anti-HBc assay on DBS is less than 100% (as indicated by the confidence interval), there is a possibility of detecting false positives, in which case the prevalence of anti-HBc would be an overestimate; this is less of an issue for HBsAg, for which confirmatory testing was undertaken.

Because there are no validated tests for DBS, we did not measure immunity (i.e. anti-HBs positivity, generally considered to be a serological marker of immunity following vaccination) or markers of recent infection. Therefore, among individuals with no evidence of HBV markers, we do not know how many are immune from vaccination. Current HBV infection is not the same as HBV incidence and we therefore cannot make assertions about new HBV transmissions. Nevertheless, incidence is likely to be low given the small pool of current infection and the high uptake of HBV vaccination.

Another limitation of this study is that the data on vaccination uptake are self-reported and may therefore be subject to poor recall or lack of understanding about which vaccinations were given. However, the findings are strengthened by the observation of a significant association between self-reported vaccination and HBV serology.

The surveys did not consistently collect information on sexual risk behaviour and therefore these were not examined. Sexual transmission is a risk factor for HBV acquisition and therefore we cannot exclude the possibility of changes in sexual risk behaviour over time. However, some studies of PWID have not found a significant association between sexual risk behaviour and HBV [11,32], suggesting that sharing needles/syringes could be the predominant risk factor for acquiring HBV in this population.

CONCLUSIONS

In Scotland, the uptake of HBV vaccination among PWID has continued to increase since the introduction of universal prison vaccination, and levels of HBV infection among PWID are low. These findings point to the success of the universal prison vaccination approach in targeting PWID, one of the risk groups specified in UK vaccination policy. The prison-based approach should be considered by countries with absent or immature universal infant vaccination programmes in order to prevent transmission among PWID and reach their WHO elimination target (95% reduction in HBV incidence) by 2030.

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Figure 1. **Self-reported uptake of at least one dose of hepatitis B vaccine among people who inject drugs (PWID) surveyed in Glasgow and Scotland.**

*restricted to those who had commenced injecting within the previous 5 years and who had injected in the last two/six months

Table 1. **Trends in the proportion of respondents reporting having been vaccinated, number of vaccine doses received, and where vaccinated, among people who inject drugs recruited via cross-sectional surveys in Glasgow/Scotland**

		Glasgow (recent-onset PWID)*						All Scotland				
		1993	1994	1999	2001-02	2008 to 2014 combined	χ^2 for trend from 1993 to 2014	2008-09	2010	2011-12	2013-14	χ^2 for trend from 2008 to 2014
Ever been vaccinated for HBV (1+ doses)**		16% (26/166)	19% (26/138)	20% (55/272)	52% (200/387)	59% (379/639)	χ^2=193·5, p<0·001	71% (1805/2537)	72% (2161/3014)	77% (1571/2049)	77% (1744/2274)	χ^2=29·0, p<0·001
Three or more doses of HBV vaccine received**†		-	-	-	62% (123/199)	81% (301/372)	χ^2=24·8, p<0.001	77% (1355/1757)	84% (1794/2132)	85% (1315/1541)	83% (1424/1713)	χ^2=20·7, p<0·001
Where vaccinated**†‡	Prison	-	-	26% (12/47)	56% (111/199)	40% (152/379)	χ^2=0·7, p=0·402	41% (736/1804)	45% (973/2159)	48% (755/1569)	41% (714/1743)	χ^2=0·3, p=0·573
	General practice	-	-	21% (10/47)	13% (26/199)	25% (95/379)	χ^2=5·4, p=0·021	33% (592/1804)	25% (544/2159)	24% (378/1569)	24% (424/1743)	χ^2=31·1, p<0·001
	Drug treatment	-	-	40% (19/47)	23% (46/199)	28% (106/379)	χ^2=0·4, p=0·539	22% (388/1804)	21% (449/2159)	23% (366/1569)	24% (417/1743)	χ^2=5·0, p=0·026
	Hospital	-	-	13% (6/47)	7% (13/199)	9% (34/379)	χ^2=0·02, p=0·882	9% (166/1804)	8% (179/2159)	9% (148/1569)	10% (182/1743)	χ^2=2·6, p=0·109
	Other	-	-	0% (0/47)	2% (3/199)	5% (18/379)	N/A	6% (112/1804)	8% (170/2159)	6% (92/1569)	7% (118/1743)	χ^2=0·03, p=0·854

*Restricted to those with less than 5 years since injecting onset and who had injected in the last 2/6 months. See methods for details.
**Excludes those who answered 'don't know' to having been vaccinated and/or number of doses received and/or where vaccinated
†Among those who reported ever being vaccinated
‡Proportions may add up to >100% as individuals may be vaccinated in more than one location

Table 2. **Trends and determinants in the uptake of hepatitis B vaccination among people who inject drugs surveyed at injecting equipment provision sites across Scotland in 2008-09, 2010, 2011-12 and 2013-14 (restricted to those who had been injecting for 10 years or less)**

		Proportion vaccinated for HBV*					OR for HBV vaccine uptake			
		2008-09	**2010**	**2011-12**	**2013-14**	**Total**	**Univariable**	**P value**	**Multivariable**	**P value**
Survey	2008-09	69% (940/1371)	-	-	-	70% (3197/4577)	Ref		Ref	
	2010	-	70% (1020/1462)	-	-		1·06 (0·90-1·24)	0·488	1·05 (0·91-1.214)	0·540
	2011-12	-	-	71% (635/898)	-		1·11 (·.92-1·33)	0·277	1·12 (0·92-1·36)	0·266
	2013-14	-	-	-	71% (602/846)		1·13 (0·94-1·36)	0·197	1·19 (1.02-1·40)	0·028
Gender	Male	70% (646/922)	71% (695/977)	72% (431/602)	70% (367/521)	71% (2139/3022)	Ref		Ref	
	Female	65% (289/443)	67% (323/481)	69% (203/295)	72% (231/320)	68% (1046/1539)	0·88 (0·77-1·00)	0·050	1·01 (0·75-1·37)	0·937
Age at interview	≤25 years	68% (235/348)	65% (222/340)	64% (110/171)	68% (112/165)	66% (679/1024)	Ref		Ref	
	26-30 years	69% (304/439)	75% (337/447)	75% (187/249)	75% (168/224)	73% (996/1359)	1·39 (1·17-1·66)	<0·001	1·09 (0·84-1·43)	0·502
	31-35 years	70% (223/319)	74% (257/349)	77% (179/233)	74% (162/218)	73% (821/1119)	1·40 (1·16-1·69)	<0·001	1·03 (0·74-1·45)	0·858
	>35 years	67% (178/265)	63% (204/326)	65% (159/245)	67% (160/239)	65% (701/1075)	0·95 (0·80-1·14)	0·596	0·76 (0·56-1.02)	0·070
Time since onset of injecting	<2 years	48% (129/268)	53% (169/320)	50% (83/166)	60% (99/166)	52% (480/920)	Ref		Ref	
	2-4 years	68% (257/376)	67% (262/392)	69% (179/261)	69% (161/233)	68% (859/1262)	1·95 (1·64-2·33)	<0·001	1·40 (1·22-1·62)	<0·001
	5-9 years	76% (554/727)	79% (589/750)	79% (373/471)	77% (342/447)	78% (1858/2395)	3·17 (2·70-3·73)	<0·001	1·84 (1·55-2·19)	<0·001
Ever prescribed methadone	No	47% (118/249)	41% (94/231)	42% (55/130)	49% (79/161)	45% (346/771)	Ref		Ref	
	Yes	73% (822/1122)	75% (926/1231)	76% (579/767)	76% (162/684)	75% (2849/3804)	3·66 (3·12-4·30)	<0·001	2·95 (2·03-4.30)	<0·001
Ever incarcerated**	No	57% (404/712)	57% (421/736)	58% (278/479)	59% (250/421)	58% (1353/2348)	Ref		Ref	
	Yes	81% (535/657)	83% (598/725)	85% (355/417)	83% (349/419)	83% (1837/2218)	3·55 (3·09-4·07)	<0·001	2·91 (2·23-3·79)	<0·001

*At least one dose of HBV vaccination. Excludes those who answered 'don't know'

**Since onset of injecting

Table 3. **Association between HBV vaccination and ever infection (anti-HBc positivity) among people who inject drugs recruited at sites that provide injecting equipment in Scotland, 2013-14.**

			Anti-HBc positive		OR for anti-HBc positivity			
		N	n	%	Univariable	P value	Multivariable (n=2286)	P value
Ever vaccinated for HBV	No	524	60	11.5	Ref		Ref	
	Yes	1729	143	8.3	0·70 (0·51-0·96)	0·027	0·60 (0·37-0·97)	0·037
	Don't know	69	7	10.1	0·87 (0·38-2·00)	0·748	1·19 (0·63-2·27)	0·589
Gender	Male	1601	160	10.0	Ref		Ref	
	Female	707	49	6.9	0·67 (0·48-0·94)	0.019	1·04 (0·68-1·58)	0·864
Age	<35	988	36	3.6	Ref		Ref	
	35+	1330	173	13.0	3.91 (2.70-5.66)	<0.001	2.48 (1.93-3.17)	<0.001
Time since onset of injecting	<10 years	872	23	2.6	Ref		Ref	
	10+ years	1441	186	12.9	5.47 (3.52-8.51)	<0.001	3.33 (1.83-6.06)	<0.001
Ever incarcerated*	No	800	37	4.6	Ref		Ref	
	Yes	1501	170	11.3	2·63 (1·83-3·80)	<0.001	2.10 (1·34-3.31)	0·001

OR: odds ratio

*Since onset of injecting

Table 4. **Association between HBV vaccination and current infection (anti-HBc and HBsAg positivity) among people who inject drugs recruited at sites that provide injecting equipment in Scotland, 2013-14*.**

			Current infection		OR for current infection			
		N	n	%	Univariable	P value	Multivariable (n=2101)	P value
Ever vaccinated for HBV	No	472	8	1.7	Ref		Ref	
	Yes	1600	14	0.9	0·51 (0·21-1·23)	0·134	0·40 (0·16-0·97)	0·043
	Don't know	62	0	0.0	N/A	N/A	N/A	N/A
Gender	Male	1461	20	1.4	Ref		Ref	
	Female	660	2	0.3	0·22 (0·05-0·94)	0·041	0·34 (0·08-1·48)	0·335
Age	≤35	957	5	0.5	Ref		Ref	
	>35	1174	17	1.4	2·80 (1·03-7·61)	0·044	1·52 (0·52-4·50)	0·447
Time since onset of injecting	<10 years	852	3	0.4	Ref		Ref	
	10+ years	1274	19	1.5	4·28 (1·26-14·52)	0·019	2·61 (0·69-9·88)	0·158
Ever incarcerated**	No	766	3	0.4	Ref		Ref	
	Yes	1349	18	1.3	3·44 (1·01-11·71)	0·048	2·43 (0·68-8·70)	0·172
Recruitment region	GG&C	767	11	1.4	1·79 (0·77-4·16)	0·173	1·28 (0·53-3·07)	0·586
	Rest of Scotland	1367	11	0.8	Ref		Ref	

GG&C: Greater Glasgow & Clyde; OR: odds ratio

*Individuals with past infection (i.e. anti-HBc positive and HBsAg negative, n=19) were excluded, thus the comparison group was anti-HBc negatives

**Since onset of injecting

Figure 1. Assoc. between univ. Hep B prison vaccination, vaccine uptake and Hep B infection among PWID